with "specifically binds" is discussed below in the section dealing with the rejections under 35 U.S.C. §112, second paragraph. Support for the term "contiguous" is found, for example, on page 13, line 15. Basis for new claims 40-43 can be found, for example on page 25, line 7. No new matter has been added by way of this amendment and, accordingly, the entry thereof is respectfully requested.

The remaining rejections are believed to be overcome by the foregoing amendments and following remarks.

Rejections Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 10-16, 25, 30, 35 and 38-39 under 35 U.S.C. §112, second paragraph, asserting that the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. The Examiner has asserted the following specific deficiencies in the claims.

A. "Hybridizing To"

The Examiner asserts that recitation of "hybridizing to" is vague and indefinite in claim 11.

Applicants traverse this rejection.

It is well-settled that absolute specificity and precision are not required in the claims. Claims need only reasonably apprize a person having ordinary skill in the art as to their scope. *Hybritech Inc., v. Monoclonal Antibodies, Inc.,* 231 USPQ 81, Fed. Cir. 1986. The second paragraph of 35 U.S.C. §112 merely requires that an applicant set out and circumscribe a particular subject area with a reasonable degree of precision such that the metes and bounds of the invention are set forth. *Ex parte Head,* 214 USPQ 551, PTO Bd. App. 1981.

However, in an effort to facilitate prosecution, Applicants have deleted the language "hybridization" from the pending claims, as suggested by the Examiner. Applicants have introduced the language "a polynucleotide that specifically binds to a polynucleotide sequence." The specification provides extensive basis for use of this

language. For example, on page 20, lines 1-12, detection of an analyte is discussed wherein a specific binding member is prepared for binding to a target analyte such as a nucleotide target. On page 20, lines 28 through page 21, line 5, a definition of "specific binding members" is discussed, wherein a "specific binding member" is a member of a specific binding pair (see also, e.g., page 22, lines 5-30; page 21, lines 16-31; and page 9, line 17, to page 10, line 5). That is, two different molecules where one of the molecules, through chemical or physical means, specifically binds to the second molecule. Specific binding pairs can include complementary nucleotide sequences. On pages 23-26, the specification describes how the sequences provided in the application may be used to produce polynucleotide sequences (for example, primers and probes; also see, e.g., page 14, lines 7-14 for definitions of primers and probes; page 26, lines 25-35 for a description of probe assays) which can be used in assays for the detection of target nucleic acids in test samples, via specifically binding the polynucleotide sequences to the target. Probes may, for example, be designed from conserved nucleotide regions of the polynucleotides of interest or from non-conserved nucleotide regions of the polynucleotide of interest. The design of such probes for optimization in assays is within the skill of the routineer. Generally, nucleic acid probes are developed from non-conserved or unique regions when maximum specificity is desired, and nucleic acid probes are developed from conserved regions when assaying for nucleotide regions that are closely related to, for example, different members of a multi-gene family or in related species like mouse and man. Numerous examples are given in the specification that would allow one of ordinary skill in the art to determine the metes and bounds of the invention (e.g., Examples 1-11, pages 55-76). For example, selection of primers for use in polymerase chain reactions is described at least on page 27, lines 1-10 and exemplary conditions (including hybridization conditions) for such reactions are described in the Examples (e.g., Examples 3, 4, 8 and 9).

Use of probes in fluorescent in situ hybridization (FISH) technology to perform chromosomal analysis is also described herein. Such an approach can be used to identify cancer-specific structural alterations in the chromosomes, such as deletions or

translocations that are visible from chromosome spreads or detectable using PCR-generated and/or allele specific oligonucleotides probes, allele specific amplification or by direct sequencing. Probes also can be labeled with radioisotopes, directly- or indirectly- detectable haptens, or fluorescent molecules, and utilized for *in situ* hybridization studies to evaluate the mRNA expression of the gene comprising the polynucleotide in tissue specimens or cells (page 26, lines 11-21; and Example 7, pages 64-65). Use of the polynucleotide sequences of the present invention in such technology is another example of specific binding of a polynucleotide sequence to a target.

The characteristics and properties of polynucleotides of the present invention for use in hybridization reactions (including probes and amplification primers) are extensively discussed in the specification in the context of specific binding (see, for example, pages 26-33). Further, examples using polynucleotides in hybridization reactions are discussed in the application, including suitable reaction conditions (e.g., Examples 5, 6, and 7, pages 62-65).

The court has consistently stated that claim language must be read in light of prior art and teachings of the specification. The standard is that the "definiteness of the language must be analyzed...in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art." *In re Moore*, 439 F.2d 1232, 169 USPQ 236 (CCPA 1971). A claim which is clear to one ordinarily skilled in the art when read in light of the specification, does not fail for indefiniteness. *Slimfold Mfg. Co. v. Kinkead Indus., Inc.*, 932 F2d 1453, 1 USPQ2d 1536 (Fed. Cir 1986).

In view of the above amendments, the teachings of the specification and the level of ordinary skill in the present art, the applicants submit that the boundaries of the claims are capable of being understood by one of ordinary skill in the art. Therefore, withdrawal of the rejection of the claims under 35 U.S.C. §112, second paragraph, is respectfully requested.

B. "Percent Identity"

The Examiner asserts that recitation of "% identity" in claims 10, 11, 15, 25, 38, and 39 is vague and indefinite. Applicants disagree with the Examiner's assessment of the level of enabling disclosure in the present applicant in regard to "percent identity." The applicants discuss the use of available programs for calculating identity or similarity between sequences in the specification (e.g., page 12, lines 5-24). Applicants submit that use of default parameters in such programs is routine and well within the abilities of one having ordinary skill in the art -- this is the manner in which the Examiner has searched the database for sequences that may correspond to the claimed sequences. Further, at the AIPLA meeting in Crystal City, Fall of 1999, Examiner John Doll stated that the USPTO policy toward claims reciting percent identity has changed and that Examiners will no longer be rejecting percent identity claims under 35 U.S.C. §112, second paragraph.

C. "At least one epitope"

The Examiner asserts that recitation of "at least one epitope" in claims 14, 25 and 30 is vague and indefinite. It is asserted that, despite definitions of "epitope" and "conformational epitope" found on page 17, line 30 through page 18, line 17, "the nature of an 'epitope' remains unclear." (Final Office Action, page 3, paragraph 4). In particular, it is alleged that all of the definitions "appear to be based on 'spatial conformations'... [yet] the invention is alleged characterized only to the extent of linear conformations." (Final Office Action, page 3, paragraph 4).

Applicants traverse this rejection.

As noted above, the standard is that the "definiteness of the language must be analyzed...in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art." *In re Moore, supra.* A claim which is clear to one ordinarily skilled in the art when read in light of the specification, does not fail for indefiniteness. *Slimfold Mfg. Co. v. Kinkead Indus., Inc., supra.*

Nothing in the recitation of "at least one epitope" would be unclear to a skilled artisan. As previously noted, the specification defines "epitope" on pages 17-18. The definitions clearly indicate that Applicants' mean epitope to include any antigenic determinant, including both linear and spatial conformations. In addition, working examples detailing how to prepare and analyze antigenic determinants are described (*see, e.g.,* Example 11a, page 71; Example 11b, page 75; and Example 13, page 78). Further, one possessing ordinary skill in the art would readily understand and interpret that epitopes can be linear or conformational so long as it is antigenic. As defined for example in the McGraw-Hill Dictionary of Scientific and Technical Terms, 5th edition (1994), an epitope is commonly understood to be "[t]he portion of the antigen molecule that determines its capacity to combine with the specific combining site of its corresponding antibody in an antigen-antibody interaction." (copy attached hereto). In addition, the Dictionary of Microbiology and Molecular Biology, 2nd edition (1987, reprinted 1996) indicates that the term epitope is understood to refer to "... any region of the [antigenic] macromolecule with the ability or potential to elicit, and combine with, specific antibody." (underlining added, copy attached hereto). Thus, in view of the teachings of the specification and teachings of the prior art, the nature of an "epitope" is clear to one skilled in the art and Applicants respectfully request withdrawal of this rejection.

In view of the above amendments, the teachings of the specification and the level of ordinary skill in the present art, the applicants submit that the boundaries of the claims are capable of being understood by one of ordinary skill in the art. Therefore, the rejection of claims 10-16, 25, 30, 35 and 38-39 under 35 U.S.C. §112, second paragraph, should be withdrawn.

Rejections Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 14, 25 and 30 under 35 U.S.C. §112, first paragraph, asserting that "[g]iven the uncertainty of what constitutes an epitope

(discussed in paragraph 4 above), one skilled in the art can not predictably make and use the claimed epitope." (Final Office Action, page 4, paragraph 6).

For the reasons detailed above and reiterated below, Applicants traverse this rejection. By law, a patent application is presumptively enabled when filed. *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971). In other words, without reason to doubt the truth of the statements made in the patent application, the application must be considered enabling. see, *In re Wright*, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) and *In re Marzocchi, supra*. Thus, the burden is on the Office to establish why the claimed invention is not enabled by the specification.

Applicants submit that the Office has not met its burden of establishing a *prima facie* case of enablement by providing acceptable reasoning that establishes non-enablement. Accordingly, Applicants request, pursuant to 37 C.F.R. § 1.104(d)(2) that the Office support their rejection with specific data and supporting affidavit.

Although the Office has not established *prima facie* non-enablement, there is ample factual evidence of record establishing the recitation of "epitope" is enabled by the claims. Applicants' specification provides a definition of "epitope" as an antigenic determinant. Both the terms "epitope" and "antigenic determinant" are well-understood to those skilled in the art and, consequently, there is no uncertainty as to what constitutes an epitope. As such, the skilled artisan can readily and predictably make and use the invention as claimed in claims 14, 25 and 30. In sum, the enablement requirement is fully satisfied and Applicants respectfully request this rejection be withdrawn.

III. CONCLUSION

Applicant respectfully submits that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

If the Examiner notes any further matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

Please direct all further communications in this application to:

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Respectfully submitted,

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